

ATTORNEY DOCKET: 66535.000004 PC



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application Number

10/549,685

Confirmation No.:

Unassigned

Applicant

Eva CAROFF, et al.

Filed

September 19, 2005

Title

GUANIDINE DERIVATIVES AND THEIR USE AS

NEUROPEPTIDE RECEPTOR ANTAGONISTS

TC/Art Unit

Unassigned

Examiner:

Unassigned

Docket No.

66535.000004

Customer No.

21967

MAIL STOP PCT

Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450

INFORMATION DISCLOSURE STATEMENT

Sir:

In accordance with 37 C.F.R. §§ 1.97 and 1.98, and in compliance with the duty of disclosure set forth in 37 C.F.R. § 1.56, Applicants submit the attached Form PTO/SB/08A (modified) for consideration and request the documents cited therein be made of record by the U.S. Patent and Trademark Office in the above-captioned application.

Several of the documents listed on the attached Form PTO/SB/08A (modified) were cited by the European Patent Office in the International Search Report, mailed on June 16, 2004, for International Application No. PCT/CH2004/000175 and in the International Search Report, mailed on August 26, 2003, for International Application No. CH4662003. Copies of the International Search Report for PCT/CH2004/000175 and CH4662003 are enclosed herein.

Applicants respectfully point out that the submission of the listed references in this Information Disclosure Statement is not an admission that they are prior art or that they are material to patentability of any claims of the application. Also, the submission of this Information Disclosure Statement is not an indication that a search has been made by Applicants.

For the convenience of the Examiner in considering the cited references, a copy of each of the cited references, other than U.S. patents and U.S. patent publications, is enclosed

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with this communication. In considering the cited references, it may be noted by the Examiner that certain of the references may contain markings, underlinings, and/or other notations. These markings, underlinings, and/or other notations are not to be construed as drawing the Examiner's attention either to selected parts or away from other parts of the cited references. Any such markings were either present on the copies of the cited references obtained by the associated individuals, or were made thereon during the study of the references by the associated individuals.

Consideration of the foregoing plus the prompt return of a copy of the enclosed Form SB/08A with the Examiner's initials in the left column in accordance with MPEP 609 are respectfully requested.

In accordance with 37 C.F.R. § 1.97(b), this Information Disclosure Statement is believed to be submitted prior to issuance of a first Office Action and within three months of the filing date of the application. Therefore, it is respectfully submitted that no fee is required for consideration of this information. However, in the event any fee is deemed necessary, the Commissioner is authorized to charge the undersigned's Deposit Account No. 50-0206.

Respectfully submitted,

HUNTON & WILLIAMS LLP

Dated:

December 19, 2005

By:

Robert M. Schulman Registration No. 31,196

Alexander H. Spiegler Registration No. 56,625

Hunton & Williams LLP Intellectual Property Department 1900 K Street, N.W. Suite 1200 Washington, DC 20006 (202) 955-1500 (telephone) (202) 778-2201 (facsimile) RMS/AHS/asc

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

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Sheet 1 of 5

DEMAS	Complete if Known	
Application Number .	10/549,685	
Filing Date	September 19, 2005	
First Named Inventor	Eva CAROFF,et al.	
Group Art Unit	Unassigned	
Examiner Name	Unassigned	
Attorney Docket Number	66535.000004	

U.S. PATENT DOCUMENTS					
U.S. Patent Document Name of Patentee or Applicant Date of Publication of Pages, Columns, Lines, Where Relevant					
Examiner Initials *	Cite No.1	Number Kind Code ² (if known)	of Cited Document	Cited Document MM-DD-YYYY	Passages or Relevant Figures Appear
	1.	4,624,956	Lazzarini, et al.	11-25-1986	
	2.	4,716,228	Scarponi, et al.	12-29-1987	

	FOREIGN PATENT DOCUMENTS							
	0.1-	For	eign Patent Do	cument	Name of Patentee	Date of Publication of	Pages, Columns, Lines, Where Relevant	
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-	3.	DE	2206385	C2	Dr. Karl Thomae Gmbh	08-16-1973		
	4.	wo	02/24192	A1	Institut National De La Sante et De La Recherche Medicale	03-28-2002		
	5.	wo	04/083218	A1	Actelion Pharmaceuticals Ltd.	09-30-2004		
	6.	GB	1,140,387		Dr. Karl Thomae GmbH	01-15-1969		
	7.	EP	0 321 191		Pfizer, Inc.	06-21-1989		

	OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS					
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	8.	YANG, et al., "Isolation, Sequencing, Synthesis, and Pharmacological Characterization of Two Brain Neuropeptides that Modulate the Action of Morphine", PNAS, Vol. 82, pgs. 7757-7761, 1985.				
	9.	ROUMY, et al., "Neuropeptide FF, Pain and Analgesia", European Journal of Pharmacology, Vol. 345, pgs. 1-11, 1998.				
_	10.	PANULA, et al., "Neuropeptide FF, A Mammalian Neuropeptide with Multiple Functions", Progress in Neurobiology, Vol. 48, pgs. 461-487, 1996.				
	11.	LAKE, et al., "IgG from Neuropeptide FF Antiserum Reverses Morphine Tolerance in the Rat", Neuroscience Letters, Vol. 132, pgs. 29-32, 1991.				

Examiner	/Manu Manohar/	Date	09/28/2008
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	12.	ELSHOURBAGY, et al., "Receptor for the Pain Modulatory Neuropeptides FF and AF is an Orpahn G Protein-coupled Receptor", The Journal of Biological Chemistry, Vol. 275, No. 34, pgs. 25965-25971, 2000.	1
	13.	SUNDBLOM, et al., "Pulsatile Secretion of Neuropeptide FF into Human Blood", Peptides, Vol. 19, No. 7, pgs. 1165-1170, 1998.	
	14.	BONINI, et al., "Identification and Characterization of Two G Protein-coupled Receptors for Neuropeptide FF", The Journal of Biological Chemistry, Vol. 275, No. 50, pgs. 39324-39331, 2000.	
	15.	KOTANI, et al., "Functional Characterization of a Human Receptor for Neuropeptide FF and Related Peptides", British Journal of Pharmacology, Vol. 133, pgs. 138-144, 2001.	-
	16.	ALLARD, et al., "Characterization of Rat Spinal Cord Receptors to FLFQPQRFamide, a Mammalian Morphine Modulating Peptide: A Binding Study", Brain Research, Vol. 500, pgs. 169-176, 1989.	
	17.	ALLARD, et al., "Autoradiographic Distribution of Receptors to FLFQPQRFamide, a Morphine-Modulating Peptide, in Rat Central Nervous System", Neuroscience, Vol. 49, No. 1, pgs. 101-116, 1992.	
	18.	GOUARDERES, et al., "Quantitative Autoradiographic Distribution of NPFF, Neuropeptide FF Receptor in the Rat Brain and Comparison with NPFF ₂ Receptor by Using [125] INVP and [125] INVP as Selective Radioligands", Neuroscience, Vol. 115, No. 2, pgs. 349-361, 2002	
	19.	LIU, et al., "Identification and Characterization of Novel Mammalian Neuropeptide FF-like Peptides that Attenuate Morphine-Induced Antinociception", The Journal of Biological Chemistry, Vol. 276, No. 40, pgs. 36961-36969, 2001.	
-	20.	LEFRERE, et al., "Neuropeptide AF and FF Modulation of Adipocyte Metabolism", The Journal of Biological Chemistry, Vol. 277, No. 42, pgs. 39169-39178, 2002.	
	21.	MALIN, et al., "Analog of Neuropeptide FF Attenuates Morphine Abstinence Syndrome", Peptides, Vol. 12, pgs. 1011-1014, 1991.	
	22.	PROKAI, et al., "Combinatorial Lead Optimization of a Neuropeptide FF Antagonist", J. Med. Chem., Vol. 44, pgs. 1623-1626, 2001.	

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	23.	MOLLEREAU, et al., "Pharmacological Characterization of Human NPFF₁ and NPFF₂ Receptors Expressed in CHO Cells by Using NPY Y₁ Receptor Antagonists", European Journal of Pharmacology, Vol. 451, pgs. 245-256, 2002.	
	24.	QUELVEN, et al., "Dissociation of Pharmacological Pro- and Anti-opioid Effects by Neuropeptide FF Analogs", European Journal of Pharmacology, Vol. 449, pgs. 91-98, 2002.	
	25.	SCHNUR, et al., "N-(5-Fluorobenzothiazol-2yl)-2-guanidinothiazole-4-carboxamide. A Novel, Systemically Active Antitumor Agent Effective Against 3LL Lewis Lung Carcinoma", J. Med. Chem., Vol. 34, pgs. 914-918, 1991.	
	26.	TANAKA, et al., "Antiplatelet Agents Based on Cyclooxygenase Inhibition without Ulcerogenesis. Evaluation and Synthesis of 4,5-Bis(4-methoxyphenyl)-2-substituted-thiazoles", J. Med. Chem., Vol. 37, pgs. 1189-1199, 1994.	
	27.	YOKOO, et al., "Synthesis of 1-Azacycloheptan-4-one Hydrochlonde", Studies on Seven-membered Heterocyclic Compounds Containing Nitrogen. I., Vol. 29, No. 5, pgs. 631-632, 1956.	
	28.	BERTZ, et al., "Organocopper Reagents in Dimethyl Sulfide", Tetrahedron, Vol. 45, No. 2, pgs. 425-434, 1989.	
	29.	BRUMMOND, et al., "α-Chlorination of Ketones Using p-Toluenesulfonyl Chloride", Tetrahedron Letters, Vol. 40, pgs. 2231-2234, 1999.	
_	30.	MIHOVILOVIC, et al., "Asymmetric Baeyer-Villiger Oxidations of 4-Mono- and 4,4-Disubstituted Cyclohexanones by Whole Cells of Engineered Escherichia coli", J. Org. Chem. Vol. 66, pgs. 733-738, 2001.	
	31.	BAIGRIE, et al., "Stereospecific Formation of Enolates from Reaction of Unsymmetrical Ketenes and Organolithium Reagents", J. Am. Chem. Soc., Vol. 107, No. 19, pgs. 5391-5396, 1985.	
	32.	DE JONGH, et al., "Synthesis of Polyspiro Compounds Consisting of Cyclohexane Rings", Tetrahedron, Vol. 20, pgs. 2553-2573, 1964.	
	33.	RADIVOY, et al., "Reduction of Sulfonates and Aromatic Compounds with the NiCl ₂ *2H ₂ O-Li-Arene (cat.) Combination", Tetrahedron, Vol. 55, pgs. 14479-14490, 1999.	

			
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First Named Inventor Eva CAROFF, et al.

Group Art Unit Unassigned

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	45.	SINGH, et al., "Synthesis & Mass Spectra of Some Substituted 2-(2'-Benzazolylamino) Pyrimidines", Indian Journal of Chemistry, Vol. 22B, pgs. 37-42, January 1983.	
	46.	PETERLIN-MASIC, et al., "A General Synthetic Approach to Novel Conformationally Restricted Arginine Side Chain Mimetics", Tetrahedron, Vol. 58, pgs. 1557-1563, 2002.	
	47.	SCARPONI, et al., "Byciclic Compounds with Potential Antiulcer and/or Antisecretory Activity", Il Farmaco, Vol. 43, No. 7-8, pgs. 575-596, 1988.	
	48.	MARINKO, et al., "A Convenient Synthesis of 4-aminomethyl-4, 5, 6, 7-tetrahydro-1, 3-benzothiazole Arginine Side-Chain Mimetics", Tetrahedron Letters, Vol. 42, No. 50, pgs. 8911-8913, 2001.	
	49.	Database Caplus 'Online! Chemical Abstracts Service, Columbus, Ohio, retrieved from STN Database Accession No. 1986:168468 XP002249435, RN 92715-48-5, 101242-99-3, 101243-00-9, 101243-32-7 and 101701-49-9 & JP 60 226810 A, Ikeda Mohando Co., Ltd., November 12, 1985.	
-	50.	Database Caplus 'Online! Chemical Abstracts Service, Columbus, Ohio, retrieved from STN Database Accession No. 1987:176383 XP002249436, RN 107880-36-4 a nd 10788-37-5 & JP 62 033158 A, Shionogi and Co., Ltd., February 13, 1987.	
	51.	Database Caplus 'Online! Chemical Abstracts Service, Columbus, Ohio, retrieved from STN Database Accession No. 1986:168468 XP002249437, RN 188611-98-5 & JP 90 059258 A, Ono Pharmaceutical Co., March 4, 1997.	
			

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